

REMARKS

Claims 1-55 are pending in the application. No amendments have been made by the present response.

Telephone Interview

Applicants thank Examiner Popa for the helpful telephone interview with Greg Hamilton and the undersigned on March 6, 2008. The obviousness rejections of the claims were discussed, but no agreement was reached.

35 U.S.C. §103(a) (Obviousness)

At pages 2-6 of the Office Action, claims 1-4, 12-17, 19-25, 32-46, 48-50, 54, and 55 were finally rejected as allegedly unpatentable over Shah, U.S. Patent No. 6,020,004, in view of Chen et al., U.S. Patent No. 6,537, 813 ("Chen") and Tice et al., U.S. Patent No. 4,389,330 ("Tice").

Independent claim 1 is directed to a process for preparing nucleic acid-containing microparticles. The method requires "continuous" action at the following steps (maintaining the lettering for the steps used in the claim): (b) continuously supplying a first emulsion to a mixing chamber; (c) continuously supplying a second aqueous solution to the mixing chamber; (d) continuously emulsifying the first emulsion and the second aqueous solution in the mixing chamber to form a second emulsion; and (e) continuously transferring the second emulsion from the mixing chamber to a solvent removal device. An aqueous suspension of nucleic acid-containing microparticles is ultimately formed in the solvent removal device in step (f) via diffusion of the organic solvent into an aqueous phase of the second emulsion.

Shah describes "an improved method for preparing polymeric microparticles containing an active ingredient through unique utilization of direct lyophilization of emulsion or suspension" (Shah at column 2, lines 56-59). The "direct lyophilization" methodology of Shah is used to remove aqueous and organic solvents and produce the microparticles (Shah at column 5, lines 63-65). According to Shah "[i]t is utilization of this single step, i.e., direct lyophilization of the final emulsion or suspension, which refines and simplifies the present process over

previously described processes, which require multiple steps and are often cumbersome”  
(Shah at column 6, line 66, to column 7, line 3).

Chen was cited as disclosing a concurrent flow mixing method and apparatus for the preparation of nucleic acid-containing microparticles. According to the Office Action, “one of skill in the art would have been motivated to modify Shah’s method by using the apparatus of Chen et al. in a continuous process” (Office Action at page 4).

Tice describes a multi-step solvent evaporation process for the preparation of microcapsules.

At page 5 of the Office Action, the Examiner stated that

although Shah et al. teach direct lyophilization as simplifying the process, Tice et al. clearly teach their method as achieving unexpectedly higher active agent loading and microparticles quality as compared to single-step methods. For these reasons, one of skill in the art would have been motivated to sacrifice simplicity for quality, in order to achieve microparticles with superior characteristics.

Applicants respectfully contest the assertion that the skilled person having read Shah and Tice would have had any reason to modify the single-step method of Shah to include the multi-step method of Tice.

Shah places a clear emphasis on the importance of using only a single step (direct lyophilization) on the final emulsion or suspension. The Background section of Shah refers to the same Tice reference (i.e., U.S. Pat. No. 4,389,330) cited in the present Office Action. In its reference to Tice, Shah states that the solvent evaporation technique (as described in Tice) “is often not preferred because active ingredient is often lost during the solvent extraction process” (Shah at col. 2, lines 11-12). In summarizing the importance of direct lyophilization to his methods, Shah states that his one-step method “provides several significant advantages over the processes described in the art” (Tice having been explicitly referenced as a prior art method) that include ease of manufacture of the active ingredient loaded microparticles, provision of sustained release formulations that maintain the activity and integrity of the active ingredient during release, and attainment of higher yields, high loading, and higher loading efficiencies (Shah at column 2, line 56, to column 3, line 5). In addition, Shah states that “the present process is more refined and simpler than those described in the art, and the activity and integrity of the active ingredient is maintained throughout the process” (Shah at column 3, lines 13-16).

Shah's comments on the advantages of its single-step direct lyophilization method as compared to the multi-step solvent evaporation process of Tice directly contradict the remarks in the Office Action alleging that Tice's methods achieve "higher active agent loading and microparticles quality" and that "one of skill in the art would have been motivated to sacrifice simplicity for quality, in order to achieve microparticles with superior characteristics." Shah clearly states that its method results in higher yields, high loading, and higher loading efficiencies. As a result, Shah teaches that its method is superior to those in the art (such as Tice) because of both (i) simplicity of manufacture, and (ii) the quality of the resulting microparticle product. Contrary to the suggestion in the Office Action, the skilled person having read the cited references would have concluded that Shah teaches methods of preparing microparticles having all-around superior characteristics (as compared to those of Tice).

In view of the teachings of Shah and Shah's direct commentary on Tice (which published about 14 years before the filing date of Shah), the skilled person would have been strongly discouraged from modifying Shah' method by adding Tice's two-step solvent removal method. Shah teaches that such a modification would have been expected to result in both a more cumbersome method as well as the production of a lower quality product. As a result, the teachings of Shah not only would have failed to provide the requisite reason for making the modification proposed in the Office Action, its comments regarding the drawbacks of Tice clearly teach away from making such a modification. "A reference may be said to teach away when a person of ordinary skill, upon reading the reference, would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant" (emphasis added). In re Gurley, 27 F.3d 551, 553 (Fed. Cir. 1994). In this case, the skilled person having read Shah and Tice would clearly have been discouraged from modifying Shah's method to include Tice's two-step solvent removal method.

In view of the forgoing remarks, applicants respectfully submit that the skilled person would have had no reason to make the modifications to Shah suggested in the Office Action. As a result, the combination of Shah, Chen, and Tice do not render obvious the claimed methods. Applicants request that the Examiner withdraw the rejection of independent claim 1 and claims 2-4, 12-17, 19-25, and 32-46 that depend therefrom.

At page 6 of the Office Action, claims 1-6, 12-17, 19-25, 32-46, 48-50, 54, and 55 were finally rejected as allegedly unpatentable over Shah taken with Chen and Tice in further view of Parikh et al., U.S. Patent No. 5,660,858 ("Parikh").

The prior non-final Office Action cited Parikh as describing the use of lipid stabilizers (recited in dependent claims 5 and 6) and asserted that "[i]t would have been obvious to one of skill in the art, at the time the invention was made, to modify the method of Shah taken with Chen et al. and Tice et al. by including lipid stabilizers".

As detailed above, the combination of Shah, Chen, and Tice does not render obvious the method of independent claim 1. Parikh provides nothing that supplements the deficiencies of Shah, Chen, and Tice or renders obvious the method of independent claim 1. Accordingly, once independent claim 1 is held allowable, all of the remaining dependent claims should also be in condition for allowance.

At page 7 of the Office Action, claims 1-4 and 7-55 were finally rejected as allegedly unpatentable over Shah taken with Chen and Tice in further view of Hartounian et al., U.S. Published Application Number 20020039596 ("Hartounian") and Hedley et al., U.S. Patent No. 5,783,567 ("Hedley").

The prior non-final Office Action cited Hartounian and Hedley as allegedly describing features of various dependent claims and asserted that it would have been obvious to modify the methods of Shah, Chen, and Tice in view of Hartounian and Hedley to arrive at the methods of these dependent claims.

As detailed above, the combination of Shah, Chen, and Tice does not render obvious the method of independent claim 1. Hartounian and Hedley provide nothing that supplements the deficiencies of Shah, Chen, and Tice or renders obvious the method of independent claim 1. Accordingly, once independent claim 1 is held allowable, all of the remaining dependent claims should also be in condition for allowance.

Applicant : Michael Tyo et al.  
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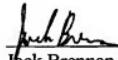
CONCLUSIONS

Applicants submit that all grounds for rejection have been overcome, and that all claims are now in condition for allowance.

Enclosed is a Petition for Extension of Time. The extension of time fee is being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Please apply any other charges or credits to deposit account 06-1050, referencing Attorney Docket No. 08191-012002.

Respectfully submitted,

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